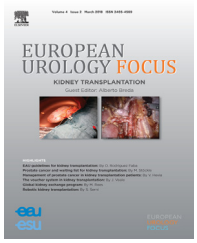
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus



Letter to the Editor

Re: Maria J. Ribal, Philip Cornford, Alberto Briganti, et al. European Association of Urology Guidelines Office Rapid Reaction Group: An Organisation-wide Collaborative Effort to Adapt the European Association of Urology Guidelines Recommendations to the Coronavirus Disease 2019 Era. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2020.04.056

Metastatic Prostate Cancer and COVID-19: Do Current Data Allow Modification of Established Treatment Recommendations?

The COVID-19 pandemic is undoubtedly challenging uro-oncologists worldwide in delivering optimal treatment for metastatic prostate cancer (mPC). The European Association of Urology (EAU) Guidelines Office Rapid Reaction Group recently published a collaborative effort on adapting the existing EAU guideline recommendations to the COVID-19 era [1]. The authors recommend avoiding taxane treatment in metastatic hormone-sensitive PC (mHSPC) and metastatic castration-resistant PC (mCRPC) as far as possible. However, docetaxel has already become a treatment standard in mHSPC and the recently published CARD study has proven the superiority of cabazitaxel over novel hormonal therapies (NHTs) for third-line treatment in mCRPC [2,3]. The primary objective of this recommendation by the guideline group is to avoid the risk of neutropenia and frequent hospital visits during the pandemic. However, neutrophils do not play a major role in antiviral immunity. There are no reports of increased viral infection rates or higher severity of viral infection among neutropenic patients besides hematological diseases that typically involve lymphocytic defects and lymphopenia, and the underlying disease renders these patients susceptible to viral infection. If the cytokine release (CR) that aggravates COVID-19 is of concern, in contrast to certain immunotherapies, there are no reports linking taxanes with systemic CR.

Moreover, the authors recommend the use of enzalutamide in mHSPC. However, enzalutamide has not yet been approved by the European Medicines Agency for this indication. Montopoli and colleagues [4] recently reported on an Italian epidemiology study showing that PC patients receiving androgen deprivation therapy appear to be partly protected from SARS-CoV-2 infection. Although limited by missing information regarding tumor stage and type of systemic treatment, these results are interesting and might support the rationale to promote treatment targeting the androgen receptor in mHSPC and mCRPC during the pandemic. It is noteworthy that several studies indicate that anti-androgen drugs could be a hypothetical treatment option for COVID-19 [5]. Indeed, androgen sensitivity might be a gateway to COVID-19 disease severity. Hoffmann and colleagues [6] demonstrated that SARS-CoV-2 cell entry depends inter alia on TMPRSS2, as it primes the spike protein of the virus. While the actual function of TMPRSS2 remains unclear, its regulation by the androgen receptor has already been shown. *TMPRSS2* gene fusions with the E26 transformation-specific transcription factor family occur frequently in PC. While TMPRSS2 expression is elevated in mHSPC, its expression in mCRPC is inconsistent, remaining an intended side effect of antiviral treatment with NHT that is at least debatable [7].

In summary, there is no foreseeable end to the COVID-19 pandemic and decisions on optimal treatment in mHSPC and mCRPC will be challenging uro-oncologist for a long time to come. At present, there are no valid data showing that NHT should be the preferred treatment option. Promising preclinical data suggest that androgen sensitivity is linked to COVID-19 disease severity by TMPRSS2 expression. However, the available data are not sufficient to dispense with taxane treatment during the pandemic. In compliance with all COVID-19 safety regulations, treatment decision-making for mPC should still be based on the well-established principles of tumor aggressiveness, comorbidity, and patient preference.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Ribal MJ, Cornford P, Briganti A, et al. European Association of Urology Guidelines Office Rapid Reaction Group: an organisation-wide collaborative effort to adapt the European Association of Urology guidelines recommendations to the coronavirus disease 2019 era. Eur Urol 2020. http://dx.doi.org/10.1016/j.eururo.2020.04.056, Apr 27:S0302-2838(20)30324-9. Online ahead of print. PMID: 32376137.

[2] Gillessen S, Attard G, Beer TM, et al. Management of patients with advanced prostate cancer: report of the Advanced Prostate Cancer consensus Conference 2019. Eur Urol 2020;77:508–47.

[3] de Wit R, de Bono J, Sternberg CN, et al. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. N Eng J Med 2019;381:2506–18.

https://doi.org/10.1016/j.euf.2020.05.018

[4] Montopoli M, Zumerle S, Vettor R, et al. Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: a population-based study (n=4532. Ann Oncol 2020. http://dx.doi.org/10.1016/j.annonc.2020.04.479, May 4:S0923-7534(20)39797-0. Online ahead of print. PMID: 32387456.

[5] Wambier CG, Goren A, Vano-Galvan S, et al. Androgen sensitivity gateway to COVID -19 disease severity. Drug Dev Res 2020. http://dx.doi.org/10.1002/ddr.21688, May 15. Online ahead of print. PMID: 32412125.

[6] Hoffmann M, Kleine-Weber H, Schroeder S, Mueller MA, Drosten C, Poehlmann S. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181, 271–80.e8.

[7] Hermans KG, van Marion R, van Dekken H, Jenster G, van Weerden WM, Trapman J. TMPRSS2:ERG fusion by translocation or interstitial deletion is highly relevant in androgen-dependent prostate cancer, but is bypassed in late-stage androgen receptor-negative prostate cancer. Cancer Res 2006;66:10658–63.

Christian Thomas*
Carsten Grüllich
Holger H.H. Erb
Department of Urology, Technische University of Dresden, Dresden, GermanyDepartment of Urology, Technische University of Dresden, Dresden, Germany

*Corresponding author. Department of Urology, University Hospital Carl Gustav Carus Dresden, Technical University of Dresden, Fetscherstrasse 74, 01307 Dresden, Germany. Tel. +49 351 4582447, Fax +49 351 4584333.
E-mail address: christian.thomas@uniklinikum-dresden.de (C. Thomas).